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Crush syndrome: a review of current knowledge and treatment strategies

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ABSTRACT

Crush syndrome is a severe systemic manifestation resulting from the breakdown of muscle cells leading to the release of toxic substances into the bloodstream. This condition can occur when a part of the body experiences a significant amount of pressure for an extended period. Crush syndrome presents with severe metabolic disruptions such as acute kidney injury, electrolyte disturbances, and cardiovascular collapse. It is essential to understand the pathophysiology and clinical features of crush syndrome for effective management and prevention of potentially devastating outcomes. The act of crushing and rupturing muscular cells generates a mechanical force that triggers the discharge of myoglobin. Subsequently, myoglobin undergoes a conversion into metmyoglobin and acid hematin, which are subsequently released into the systemic circulation. The muscular tissue harbors a variety of electrolytes and enzymes, which may attain toxic levels upon entry into the circulation in excessive quantities. The release of sodium, calcium, and fluids due to regional ischemia leads to increased muscle volume and tension, depletion of creatine kinase (CK) and ATP, and muscle vasodilation, further exacerbating hypotension. Crush syndrome can also lead to cardiovascular instability and renal failure due to vasomotor and nephrotoxic factors. Elevations in serum CK levels exceeding 1000 IU/l, along with accompanying clinical features, are widely recognized as indicative of crush syndrome. Diagnostic investigations commonly involve assessing serum levels of aldolase, myoglobin, and myoglobin degradation products. Progressive increases in serum levels of lactic acid, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH) are observed, while levels of serum urea and creatinine exhibit a steep rise, particularly following prolonged compression, and serve as valuable predictors of renal failure. The treatment of crush syndrome requires a multidisciplinary approach that addresses the metabolic, cardiovascular, and renal complications associated with this condition. The mainstay of treatment includes early release of the affected limb or compartment, fluid resuscitation, correction of electrolyte abnormalities, and alkalinization of urine. Additionally, renal replacement therapy and hyperbaric oxygen therapy may be beneficial in managing acute kidney injury and tissue hypoxia, respectively. Crush syndrome, albeit infrequent, represents a potentially fatal medical condition that demands a thorough comprehension of its underlying pathophysiology, clinical manifestations, and treatment modalities. Early recognition and appropriate management of this condition can significantly reduce morbidity and mortality associated with crush syndrome.

Keywords: Crush syndrome, rhabdomyolysis, myoglobin, renal failure

INTRODUCTION

Crush syndrome is a rare but potentially life-threatening condition that occurs when a significant amount of pressure is applied to a part of the body for an extended period, leading to muscle injury and the release of toxic metabolites into the bloodstream. Crush injury, resulting from compressive forces, can be a severe and potentially life-threatening condition. Although it is primarily a localized injury to the affected body part, it can have systemic effects as well. Crush syndrome, also known as traumatic rhabdomyolysis, is a rare but severe systemic manifestation that occurs as a result of the breakdown of muscle cells, leading to the release of their contents into the bloodstream. This release of toxic substances, including myoglobin, can lead to severe complications such as acute kidney injury, electrolyte disturbances, and cardiovascular collapse. Understanding the pathophysiology and clinical features of crush syndrome is crucial for effective management and prevention of potentially devastating outcomes.[1,2] Despite being acknowledged by German physicians during the First World War and following the Messina earthquake of 1909, it was not until 1941 that the first documented account of crush syndrome in English language literature was reported by Bywaters and Beall.[3] Crush injuries are frequently encountered during natural disasters, such as earthquakes. Nevertheless, emergency physicians more commonly encounter crush syndrome in individuals who have been involved in motor vehicle collisions, particularly

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those with prolonged extrication times, and those who are victims of physical assaults.[4] The terminologies related to crush injury encompass a spectrum of conditions. "Crush injury; refers to the direct physical damage caused to the muscles as a result of external pressure. Crush syndrome; also known as rhabdomyolysis, is a severe manifestation of muscle injury caused by disruption of cellular integrity and release of muscle contents into the bloodstream. Compression syndrome; on the other hand, occurs when there is an indirect injury to the muscle caused by a slow compression of a muscle group leading to ischaemic damage and subsequent release of crush substances into the circulation. Finally, compartment syndrome is a localized and rapid rise of tension within a muscle compartment leading to metabolic disturbances similar to those seen in rhabdomyolysis."

PATHOPHYSIOLOGY

Crush injuries may lead to fatal consequences, with a high percentage of patients succumbing to head injuries or asphyxiation. Only a fraction of patients that make it to the hospital experience a successful recovery, with the remaining percentage developing crush syndrome, which presents with severe and extensive metabolic disruptions. It is therefore critical for medical professionals to prioritize and implement effective treatment approaches to address the complex and life-threatening complications associated with crush syndrome.[5,6] The mechanical trauma resulting from crush and rupture of muscular cells provokes the extrusion of myoglobin, which undergoes subsequent conversion into metmyoglobin and subsequently acid hematin before entering the systemic circulation. Muscles contain various electrolytes, such as potassium, magnesium, phosphate, acids, and enzymes including CK and lactate dehydrogenase (LDH). Although these are necessary for cell function, they become toxic in the circulation when released in excessive amounts. Regional ischemia occurs in crush syndrome due to the obstruction of micro and macrocirculation in the muscles, prompting the release of sodium, calcium, and fluids, resulting in increased muscle volume and tension. This process leads to the depletion of CK and ATP. Moreover, the activation of the nitric oxide system leads to muscle vasodilation and further exacerbates hypotension.[7] Crush syndrome can lead to cardiovascular instability which may have several underlying causes. The translocation of fluids from the extracellular compartment towards the injured muscular cells may induce depletion of intravascular volume, culminating in the development of hypovolemic shock. Additionally, cardiovascular compromise can arise from blood loss associated with the injury, as well as myocardial toxicity resulting from electrolyte disturbance. Moreover, experimental models have demonstrated that substances released by the muscular cells are capable of inducing direct depression of the cardiovascular system.[8] The most severe complication of crush syndrome is renal failure.[9] The pathogenesis of renal failure in crush syndrome is intricate and entails the interplay of vasomotor and nephrotoxic factors.[10]

INVESTIGATIONS

Studies have demonstrated a strong association between the elevation of CK and the development of renal failure as well as mortality in patients with crush syndrome.[11] An elevation in serum CK levels exceeding 1000 IU/L, in conjunction with relevant clinical features, is frequently considered diagnostic of crush syndrome. The normal range for CK levels is 25-175 U/L, which typically starts to rise within 2 to 12 hours following a crush injury, peaks between 1 to 3 days, and then gradually declines after 3 to 5 days. Additional investigations that may assist in diagnosing crush syndrome include measurement of serum aldolase levels. Serum myoglobin and its degradation products are highly sensitive laboratory tests for detecting the release of muscle proteins into the systemic circulation. Additional biomarkers that exhibit a progressive elevation comprise serum AST, ALT, lactic acid, and LDH. Moderate increments in serum uric acid may also be detectable. Serum urea and creatinine concentrations show a sharp surge, particularly following an extended period of crush, and serve as valuable predictors of renal failure. Additionally, an early increase in serum potassium levels can serve as a predictor for dialysis.[12] In crush syndrome, there may be a concomitant occurrence of hypocalcemia and stress-related hyperglycemia. Presence of myoglobin products in urine can be detected by urine RE. In addition, blood gas analysis, complete blood cell count, and electrocardiography are indispensable diagnostic modalities. Intracompartmental pressure monitoring is crucial, as readings surpassing 30 mm Hg warrant the performance of fasciotomy. Doppler ultrasonography is conducted to detect limb ischemia, and the body weight of the patient is documented.[13]

TREATMENT STRATEGIES

The immediate treatment of individuals affected by crush injuries is crucial to minimize morbidity and mortality. The possibility of concurrent injuries such as fractures, spinal or solid organ damage should be considered and managed accordingly after the assessment of airway, breathing, and circulation. Prompt oxygen administration and control of any visible bleeding should be prioritized. The provision of fluid therapy, either parenteral or enteral, contingent on resource availability and the extent of the casualties, is essential to sustain intravascular volume. Nevertheless, parenteral therapy is usually the preferred mode of administration. Swift evacuation to a facility with definitive care is imperative. Upon admission, patients must undergo hourly urine output measurements, electrolyte surveillance, arterial blood gas analysis, and monitoring of muscle enzymes. Central venous pressure and invasive arterial monitoring should be taken into consideration. Prevention of acute kidney injury is paramount, as its occurrence is linked to reduced survival rates.[9,14] Resuscitation for crush syndrome ideally starts at the site of injury, as casualties are often in shock and may lose significant amounts of extracellular fluid into the injured extremity. In combat scenarios, obtaining a comprehensive patient history may not always be feasible, and the syndrome can progress surreptitiously in patients who seem initially stable. Hence, personnel must receive adequate training to identify the condition promptly and manage it proactively with fluid therapy. The recognition and management of crush syndrome mandate close collaboration among anesthesiologists, trauma surgeons, biochemists, physicians, and radiologists.

The choice of fluid administered in prehospital settings is determined by local resources and protocols for fluid replacement., prehospital vehicles typically carry saline as the preferred fluid, which was recommended for use in

crush injuries during a recent consensus meeting.[15] The administration of solutions containing potassium carries a theoretical disadvantage, as it may exacerbate hyperkalemia. The amount of fluids administered varies greatly, with reports of infusion of more than 25 liters of saline in a single day. While there is agreement on the use of saline as the preferred fluid, in order to address metabolic acidosis, supplementation with bicarbonate, lactate or even oral citrate is necessary. Alkalinization treatment, also known as bicarbonate therapy, has been proposed as a potential treatment for crush syndrome. Gunal et al recommend the administration of 50 mmol of bicarbonate per liter of isotonic saline.[16] It is widely recognized that substantial quantities of fluid may accumulate within the traumatized muscle, with as much as 12 liters in the initial 48 hours for an adult weighing 75 kilograms. To reduce the salt burden, Better advises an initial infusion rate of 1 to 1.5 liters of saline per hour, followed by 5% glucose.[17] The patient's central venous pressure (CVP), blood pressure (BP), pulmonary status, and urinary output are closely monitored. An insulin glucose drip may be administered to mitigate a sharp increase in serum potassium concentration. In cases of crush syndrome, patients often require multiple blood product transfusions, and it is important to properly address the logistical challenges associated with collection, storage, and transportation.[18]

Diuresis

It is important to emphasize that preserving optimal kidney function is a critical component of managing crush injuries. In situations where crush syndrome has been confirmed, urinary output must be upheld at a minimum rate of 300 ml/hr, corresponding to a minimum fluid intake of 12 liters daily, given that fluid accumulation within the injured muscles may amount to as much as 4 liters.[18] There is a divergence of opinions regarding the necessity of inducing diuresis versus maintaining sufficient hydration to prevent renal failure. While some experts advocate that administering mannitol is unnecessary and that adequate fluid replacement and alkalinization suffice, others contend that mannitol may offer additional benefits beyond its diuretic properties.[16] Holt et al. suggest that while mannitol is indicated for use in cases of compartment syndrome, it is not superior to intravenous fluids alone.[19]

Dialysis

The diagnosis of acute kidney injury (AKI) was established using the Kidney Disease Improving Global Outcomes (KDIGO) composite staging criteria. This involves an increase in serum creatinine of 0.3 mg/dl or more within 48 hours or a reduction in urine output below 0.5 ml/kg/h for six hours, in the absence of pre-existing renal disease. Significant predictive factors for requiring dialysis comprise anuria, fluid overload, levels of serum creatinine, blood urea nitrogen (BUN), and bicarbonate levels.[16] Additionally, elevated potassium levels above 7 meq/1 are an important independent predictor for dialysis. In some cases, dialysis may need to be performed two to three times daily for up to 15 days. Patients at high risk for hyperkalemia may require prophylactic dialysis.[20]

Renal Replacement Therapy

Renal replacement therapy (RRT) is a crucial component of the management of AKI in crush syndrome patients. Crush syndrome-induced AKI results from the release of myoglobin into the circulation, leading to acute tubular necrosis and renal failure. RRT aims to remove the toxic substances, maintain fluid balance, and correct electrolyte imbalances in patients with AKI.[21] A study conducted by Ishii et al. in 2020 found that early initiation of continuous RRT in patients with crush syndrome-associated AKI significantly improved renal recovery and overall survival.[22] A study published in the Journal of Trauma and Acute Care Surgery found that early initiation of renal replacement therapy (RRT) in patients with crush syndrome and AKI can improve overall outcomes, reduce complications, and decrease mortality rates.[23]

Moreover, some researchers have suggested that extracorporeal membrane oxygenation (ECMO) may have a role in the management of crush syndrome-induced AKI. A recent study reported successful ECMO support in a patient with severe crush syndrome complicated by AKI and respiratory failure.[24] However, further studies are required to determine the optimal timing and duration of ECMO in this setting.

In conclusion, RRT plays a crucial role in the management of AKI in crush syndrome patients. Early initiation of continuous RRT may improve renal recovery and overall survival. High-volume hemofiltration has also been shown to be effective in removing circulating myoglobin. While ECMO may have a role in managing AKI in these patients, further research is needed to determine its optimal use.

Hyperbaric Oxygen

Exposure to high pressures has been shown to increase the physically dissolved levels of oxygen in the plasma, resulting in improved tissue viability, mild vasoconstriction, and reduced fluid outflow from the vascular compartments, thereby decreasing tissue edema. This process directly benefits wound healing by promoting fibroblast proliferation. Moreover, exposure to high pressure has the potential to decrease anaerobic bacterial growth in necrotic muscle.[25] Typically, the standard treatment involves exposure to 2.5 atmospheres of pressure for approximately one and a half hours, administered twice a day for a duration of one week.[26]

CONCLUSION

In conclusion, crush syndrome is a serious medical condition that can result in significant morbidity and mortality if not managed appropriately. The initial assessment of patients with suspected crush injury should focus on timely extrication and provision of effective fluid resuscitation. The maintenance of effective kidney function is critical in the management of this condition, with measures such as prophylactic dialysis and the administration of mannitol potentially playing a key role. The importance of close monitoring and management of electrolyte imbalances, particularly hyperkalemia, cannot be overstated. The use of hyperbaric oxygen therapy and other advanced wound care techniques can aid in tissue healing and may prevent the need for amputations. Overall, early recognition and aggressive management of crush syndrome are essential to improve outcomes and minimize complications in affected patients.

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